do not ascribe the great practical importance to them that Dr. Savage does; that is purely a matter of individual experience and judgment.

The small chapter on routine in eye work is interesting because it gives one the routine procedures of a practitioner of as long experience and of as high a standing as Dr. Savage. For those doing eye work as a specialty there is nothing to be learned from it, however, as we all have to adopt our own routine as our character, temperament and training leads us to it.

H. B.

Handicraft for the Handicapped. By Herbert J. Hall and Mertice M. C. Buck. New York: Moffatt, Yard & Co. 1916.

A book written from practical experience is always of value and especially on this important subject of employment for those of our patients who are suffering from nothing to do. This book very fully describes the essential points for the casual reader on the subject, and also many of the more detailed directions for the teacher or the patient. The variety of subjects covered enables us to choose the one most adapted to our individual needs.

Parts of the work as here described could be applied to cripples, convalescents from acute or chronic diseases not able as yet to go back to hard work, tuberculous patients in an arrested stage, neurasthenics and some with more serious mental deficiency.

The authors take up the subjects of basketry, chair-seating, netting, weaving, bookbinding, cement-working, pottery, and light blacksmithing, and have appended a very considerable reference list of books going into more detail on many of these subjects. In the chapter on basketry details are given as to the kind and size of reeds to use, how to prepare them for use and diagram illustrations of just how to weave them to produce certain baskets and forms. Pictures are shown that make chair-seating appear very easy. Different knots employed in netting and numerous suggestions as to articles that can be made are of help in that section. Weaving requires a larger apparatus than some of these other arts, but this too is carefully described. Bookbinding, although quite a complex process, is carefully outlined and pictured. In this, as in the other arts and crafts, a little practical instruction will aid materially the suggestions in this book. There is considerable difference between cement work and pottery, the former requiring no kiln or expensive lathes and consequently producing a cruder, but a nevertheless, serviceable set of articles. Blacksmithing does not refer to shoeing horses, but to making useful household wares, such as andirons, pokers, heavy latches, etc.

And so readers of this book will find that Dr. Hall and Mertice Buck have from their own experience at Devereaux Mansion, Marblehead, and elsewhere, suggested many practical occupations that are a pleasure as well as a stepping stone to self-reliance and health.

P. H. P.

DEPARTMENT OF BACTERIOLOGY AND PATHOLOGY.

(Edited by Benjamin Jablons, M. D., San Francisco.)

[This department has as its chief object the dissemination of the special knowledge that is being developed in the scientific laboratories of the world, and which are of practical interest to the medical practitioner. Abstracts of general articles will be published from time to time as well as preliminary reports of subjects that are of universal interest.]

Complement Fixation for Tuberculosis.

To appreciate the factors entering into the Complement Fixation Reaction for Tuberculosis it is necessary to keep two points in mind; first, the reaction of the human organism to the tubercle bacillus and its derivatives and, second, its reaction to the tissue products resulting from the action of the tubercle bacillus. It is known that the introduction of the foreign protein of whatever nature into the body calls a specific and non-specific response. The specific reaction is that evidenced by the mobilization of an antibody, whose nature may be that of either an agglutinin, a precipitin, a bacterictroptin, an opsonin, a bacteriolysin or a complement fixing antibody. Then the non-specific antibodies may also be mobilized and these are chiefly of the ferment and anti-ferment variety. In order therefore to diagnose the presence of an organism that is sufficiently active to call forth a response from the infected body, it is necessary to seek for one or even all of these antibodies.

Datta, in an article published July, 1915, in the Policlinico, summarizes his studies in sixty tuberculous patients in whom parallel observations were made of a skin tuberculin reaction, agglutination precipitin and complement fixation test, using two different technics for the latter. He found that the skin tuberculin reaction was the most constant in all cases of pulmonary tuberculosis, excepting those that were more advanced. The fixation of complement came next in order of frequency and was most constant in the graver cases. The agglutinins and precipitin tests never gave independent positive findings but trailed the others, giving positive findings occasionally in the milder cases. He advises for diagnosis and prognosis of tuberculosis, that the skin tuberculin test plus the complement fixing reaction be employed. Krause's recent publications on the studies of the skin reaction in the immunized guinea pigs conclusively prove the contention of many observers that the supersensitiveness to tuberculo protein after pre-existing infection is never entirely lost even after healing excepting in the presence of intercurrent diseases. This naturally increases the limitations of this test as a diagnostic factor for the determination of an early active tuberculosis.

Theobald Smith, in a recent number of the Journal A. M. A., states that agglutinins and precipitins are constant in spontaneous infections with the tubercle bacillus; the opsonins are, however, slightly reduced or fluctuating. Complement fixing bodies are never present in healthy individuals, but occur in 68% of those infected. This has been disproved by most of the recent work. Opsonin determinations have been discarded since the early reports of Wright owing to their inconstancy and the fluctuations produced by autoinfection.

Complement deviation still remains the most delicate test for the detection of the presence of an antibody producing substance. Its delicacy is such that even minimal amounts of proteins can be recognized when brought in contact with their specific antibodies in the presence of complement. This accounts for the strenuous efforts immunologists have made to apply this test to the diagnosis of tuberculosis since Bordet and Gengou first described their phenomenon.

A great deal of interest has been aroused recently in the subject owing to the fact that several investigators claim to have attained the goal which they had been striving for since the earliest reports of the work of Wassermann and Bruck. The chief difficulty was to obtain a suitable antigen which would react with the antibodies produced as a result of an infection with the tubercle bacillus. This if obtained would solve the problem of early diagnosis of tuberculous infection and also determine whether a definite cure was present. The difficulties encountered can best be seen from a review of some of the work of various investigators. In the early days of the test the various

preparations of tuberculin were used, although in 1901 Widal and Lesmond, who first carried out complement fixation tests on tuberculosis, used homogeneous emulsions of tubercle bacilli of the A. C. type. Old tuberculin which, as you know, is practically a fifty per cent. glycerin extract of the soluble products of the metabolism of tubercle bacillus, was used by Wassermann and Bruck in the demonstration of the antibody after tubercular infection, but gave no satisfactory results in diagnosis.

Bacillus emulsion consisting practically of the insoluble components of the tubercle bacillus was used, but the results obtained were of no great value because the early cases failed to react. This manifestly rendered this substance a poor antigen for this method of investigation.

The detection of the antibody developed by the human organism against infection with tuberculosis is surrounded with many difficulties. Present knowledge justifies the assumption that there are several antibodies developed against tubercular infection. Bergel, who studied the effect of the lytic substances within the peritoneal cavity of the white mouse upon the tubercle bacillus, claims that the bacillus is made up of several layers, the first being a wax-like mantel which is strongly acid and alcohol resistant. Beneath this mantel there is another layer which consists for the greater part of a mixture of lipoids and fatty acids which contain wax granules. Within these layers there is another layer consisting entirely of neutral fat which is arranged in rows of granules bound together by thin fibers. Beneath this the albuminous nucleus of the tubercle bacillus rests, and according to Bergel, each of these layers has a different staining reaction and a different chemical composition, thus we can see that the body must react by the production of the tubercle bacillus. In addition it may be supposed that the necrotic caseated focus represents a foreign body from the standpoint of tissue cells and probably calls forth the production of antibodies. These features explain the varied attempts upon the part of many investigators to produce a suitable antigen to determine the presence of complement fixing bodies in the circulating blood.

Much's work was based practically on this principle, and Much on this basis prepared four partial antigens, the first being lactic acid extract, second an alcoholic, third an ether extract, and finally fourth, the protein residue. The lactic acid extract was discarded, but the three remaining antigens were used. These antigens failed to give constant results, some tuberculosis sera reacting with one, while others would react with another of these antigens. The only fact of interest is that Much, in immunizing animals and individuals, drew the conclusion that there was no humoral immunity present in tuberculosis, but that it was chiefly of a cellular nature. In other words, antibodies were not thrown out into the blood stream excepting when an excessive reaction to the bacillus had taken place. His results prove that the partial antigens are similarly of very little value in the early diagnosis of the disease, although it opens up an interesting line of investigation into the human body's immense response to tuberculosis.

Besredka in 1913 published his results in tuberculosis fixation, using as an antigen a filtrate derived from a medium consisting of a mixture of bouillon, egg-white and egg-yolk, in which tubercle bacilli were grown. His results were most encouraging excepting for the fact that the samples of tuberculin obtained in this way varied in their antigenic qualities. Another source of error was that this antigen gave cross-fixation with leutic sera. This was at first thought to be due to the lipoids contained in the media, but Brofenbrenner, who is foremost among those who have investigated this antigen in the United States, found that positive reactions occurred with certain syphilitic sera even after the lipoids had been extracted from it. Brofenbrenner has also recently proven that a syphilitic serum after being brought in contact with antilipotropic substances which will absorb these will subsequently give a fixation with the Besredka tuberculin which argues for the specific nature of the test. Inmann, Kuss, Leredde and Rubenstein found this antigen to be non-specific.

Calmette and Massoll in 1912 devised a water and peptone soluble antigen which gave very reliable results. The water soluble extracts give fixation in the late stages of the disease, whereas, the peptone soluble extracts gave fixation in the early stages of the disease.

Stimson of the Public Health Laboratories is perhaps the only one of the American investigators previous to 1915 whose investigations of the subject have gained any attention. Stimson had undertaken a fairly extensive and thorough trial of the Besredka and Calmette peptone-water soluble extracts and his conclusions are as follows:

Depending upon the antigen and the technic employed, the proportion of tuberculosis cases where positive fixation will be demonstrated will vary from a maximum of some 95 per cent. down to a much lower figure. While these antigens and technics giving the higher percentage of positive results are more valuable in confirming suspected and detecting unsuspected cases, they tend to approach such tests as that of the von Pirquet in failing to afford much information as to the stage, extent and activity of the tubercular process, nevertheless the continued presence of reactive bodies in the serum of a given patient on repeated examination, when no antigens have been artificially administered is, he believes, strong presumptive evidence of continued or recent activity of the lesions. It is striking that the antigens employed seem to have given excellent results in the hands of the original investigator, but in many instances these results could not be confirmed when used by other workers.

Among other antigens are to be mentioned the alcoholic antigen of Dudgeon, Meek and Weir, and Hirschfelder's pepsin antigen as well as the tissue antigens prepared from normal and tubercular tissues. According to many workers the least criticized antigen is an emulsion of living virulent tubercle bacilli which obviates the occurrence of non-specific reaction. These constitute the basis for the antigens used by Caulfield, Laud, Fraser, McIntosh, Filde, Radcliffe and others.

Irons and Nucoll used autolyates in the sero diagnostic test of gonorrhea. This has led Corper of the Municipal Sanatorium of the City of Chicago to seek products derived from autolysis of tubercle bacilli as antigen for this test. He found that liberation of nitrogenous substances after eight to ten days' incubation reached its maximum on the tenth day, and that the anticomplementary titre as well as the fixing titre increased from day to day up to the tenth day. At that time one one-hundredth of the original titre of the emulsion was found sufficient to bind the complement into the presence of tuberculous sera. He carried out a series of tests in 361 persons and found that the complement fixation test with autolysate antigen for tuberculosis is not absolute, being positive in about 30 per cent. of all the clinically definite cases of both active and inactive tuberculosis, and concludes that the value of the complement fixation test for tuberculosis lies in the fact that, taken in conjunction with other findings, a definitely positive reaction makes the diagnosis of tuberculosis certain. It is of value also from a differential diagnostic standpoint in that it indicates tuberculosis, when positive, as against syphilis, carcinoma, ab-

scess of the lung, empyema from other causes, bronchiectasis, etc.

The practical absence of a reaction in non-tuberculous cases makes this test, when positive, of far greater value in the diagnosis of tuberculosis than any of the biologic tests for tuberculosis thus far discovered. A positive test was never obtained in the absence of a positive von Pirquet reaction, but a large percentage of clinically normal individuals giving positive von Pirquet reactions were negative in fixation tests.

Craig modified the Besredka antigen by growing his bacilli in an alkaline egg broth and then extracting it with alcohol. The difference consisted largely in that the antigen was an alcoholic extract of the bacilli plus the medium in which they were grown minus the insoluble residue and precipitate left after extraction. In his last communication on this subject, he had modified his medium, growing tubercle bacilli on the surface of Bedders starch medium and subjecting it then to the same procedure as in his original communication. Since his results are very striking, it may be of interest to state them here. He tested 209 cases of tuberculosis of which 183, or 37.5 per cent., gave a positive reaction, and 26, or 12.4 per cent., gave a negative reaction. In 159 cases there was absolute inhibition while in 24 there was almost complete inhibition. He found 65 per cent. of fixations in cases considered inactive and argues that the test indicates the fallaciousness of clinical signs in determining whether a patient is to be considered an arrested or a cured case of tuberculosis. He states that many of these patients formerly considered cured but who since gave positive fixations, have developed symptoms. He obtained the highest percentages of cases in active infections in the moderately advanced class of patients, totaling 98.3 per cent. of those examined. Inactive cases gave 67.7 per cent. fixation and over 80 per cent. of these individuals he claims have relapsed clinically. In the far advanced cases his results are 96.4 per cent. positive fixations as compared with 96.7 per cent. in the moderately advanced, and 98.3 per cent. in the incipient cases. He claims that the method is of distinct clinical value, and does not give fixation with clinically non-tubercular or syphilitic sera. The most encouraging results, however, are those reported by Miller, who in conjunction with Zinsser, has employed an antigen prepared by triturating living or dead bacilli with dry crystals or ordinary table salt and then adding distilled water up to isotonicity. Although many antigens have given favorable results, Miller considers that the antigen they have reported is superior to the others in use, because it has failed in their hands to give cross-fixation with luetic sera, has usually been negative in arrested cases, and has been almost invariably positive in active cases. It seems also to be one more easily prepared.

It is seen, therefore, that efforts at the recognition of complement fixing bodies have been directed first against those produced by the whole bacillus, then by tuberculins, then by split products of the tubercle bacillus, and finally by what is called tissue antigens. A fairly complete summary published by Miller showed that the latter group when prepared minus tuberculins gave uncertain results. Where tuberculin was used there was also a margin of error which rendered the test of doubtful value. The antigens made up of bacillary suspensions also gave good results but a few observers have reported positive fixations with clinically arrested cases. The antigens made up of split products gave non-specific fixations with normal non-tuberculous individuals.

It is not necessary to recapitulate all of the results obtained. It suffices that up to the present time the best results have been reported with the antigens of Calmette and Massol, which contain endobacillary substances extracted by water and peptone water, the tuberculin of Besredka, which is the filtrate of an excellent culture medium for tubercle bacilli, but which is not always specific, and the salt extracts of Miller and Zinnsser, as well as the alcoholic extracts of Craig. In addition Petroff has prepared antigenic substances of bacilli grown on his gentian violet medium which he has separated into a lipoid and protein fraction which he claims gives satisfactory results. This is quoted in an article by Webb in the February number of the Journal of Laboratory and Clinical Medicine, who concludes also that the antigens of Calmette and Massol and those of Miller and Zinsser have proven reliable in cases carefully controlled by clinical diagnosis and by X-ray plates. In the last article published by Miller in the J. A. M. A. he gives the results of observations made upon 1000 cases. They were as follows: 284 cases of pulmonary tuberculosis gave positive reactions in 275, and negative in 9. Second, non-tuberculous and normal patients react negatively 144 cases; 243 Wassermanns all negative except 7, and in these 7 tuberculosis was established in 5 and not excluded in the other 2. The test was negative in arrested and in negative cases. Of 113 tested, 103 were negative and 10 positive. As a result of his studies he believes that there are cases of tubercle bacillus carriers and that the expectoration of tubercle bacilli is no indication of the activity of the disease.

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DEPARTMENT OF PHARMACY AND CHEMISTRY.

Edited by FRED I. LACKENBACH.

(Devoted to the advancement of Pharmacy and its allied branches; to the work of the Council on Pharmacy and Chemistry of the American Medical Association, and to matters of interest bearing upon therapeutic agents offered to the medical profession. The editor will gladly supply available information on subjects coming within the scope of this Department.)

NEW AND NONOFFICIAL REMEDIES.

Since publication of New and Nonofficial Remedies, 1917, and in addition to those previously reported, the following articles have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion with "New and Nonofficial Remedies":

Tablets Sodium Chloride and Citrate-Squibb (Dr. Martin H. Fischer).—Each tablet contains sodium chloride 1 gm. and sodium citrate 2 gm. E. R. Squibb and Sons, New York.

Optochin.—Ethyl-hydrocupreine.—A synthetic alkaloid closely related to quinine. It has the antimalarial and anesthetic action of quinine, but toxic symptoms, such as tinnitus, deafness, amblyopia or amaurosis (retinitis) are more liable to occur than with quinine. Investigations indicate that the drug may be of value in the treatment of lobar pneumonia, when its safe dosage has been determined.